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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/770,770	01/25/2001	Philip S. Bernard	A-68556/RFT/JJD	7770

7590 07/15/2003

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EXAMINER

TUNG, JOYCE

ART UNIT	PAPER NUMBER
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1637

20

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/770,770

Applicant(s)
Bernard et al.

Examiner
Joyce Tung

Art Unit
1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 2, 2003
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other: _____

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DETAILED ACTION

Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/02/2003 has been entered. Claims 1-16 are pending.
2. Rejections and/or objected from the previous office action are hereby withdrawn. The following rejections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.
3. Applicant's arguments filed 5/2/2003 with respect to claims 1-16 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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5. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-5 are vague and indefinite because of the first phrase of "each of said at least two probes" is redundant. Clarification is required.

b. Claims 1-16 are vague and indefinite because the claim language does not clearly indicate that $\Delta\Delta T_m$ is determined. The claim language "determining the difference in determine ΔT_m between overlapping probes as an indication...in said target nucleic acid as compared to said control nucleic acid" in claims 1 and 6 is unclear as to determine $\Delta\Delta T_m$. Clarification is required.

c. Claims 6-16 are vague and indefinite because it is unclear which set of probe hybridizes to the target nucleic acid and which set of probe hybridizes to the control nucleic acid. Clarification is required.

d. Claim 8 is vague and indefinite because it is unclear whether the difference in ΔT_m between at least two overlapping probes indicates the location in the control nucleic acid of a nucleotide which is different from the target nucleic acid. Clarification is required.

e. Claim 12 is vague and indefinite because it is unclear how ΔT_m is determined based upon the two probes from said first set of probes and one probe of a second set of probes on the control nucleic acid.

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Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guo et al. (Nature Biotechnology, 1997, Vol. 15, pg. 331-335).

Guo et al disclose the differences in thermal stability (ΔT_m) between hybrids formed with normal and single-nucleotide-variant DNA targets which are increased by as much as 200% over conventional hybridization and this increases the discrimination of single nucleotide polymorphisms in DNA hybridization (See pg. 331, the Abstract). Guo et al further disclose that the T_m s of 20mer duplexes containing 0, 1, 2, or 3, adjacent mismatches were determined (See pg. 331, fig. 2). The differential in melting temperature is greater for 1 vs 2 (60°C vs. 47°C) than

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for 0 vs. 1 (65°C vs. 61°C), suggesting that use of a purposely mismatched base in the probe hybridization increases the ability to discriminate point mutations (See pg. 332, column 1, last paragraph). Guo et al. herein, indicate that the ΔT_m of 1 mismatch vs 2 mismatch is 13°C which is greater than the ΔT_m for 0 vs. 1 mismatch which is 4°C. Thus, Guo et al. applied the concept of $\Delta\Delta T_m$ to suggest that there is the ability to discriminate point mutations by $\Delta\Delta T_m$ (Also see pg. 333, column 1, second paragraph).

Guo et al. do not disclose using a plurality of nucleic acid probes which are complementary to different overlapping region of control nucleic acid and target nucleic acid.

One of ordinary skill in the art at the time of the instant invention would have been motivated to apply the teachings of Guo et al. to identify a sequence alteration in a target nucleic acid as compared to a control nucleic acid with a plurality of nucleic acid probes. Guo et al. indicate the differences in thermal stability between hybrids formed with normal and single-nucleotide-variant DNA targets are increased by as much as 200% conventional hybridization and this increases the discrimination of single nucleotide polymorphisms in DNA hybridization (See pg. 331, the Abstract) and two probes were used to determine the melting temperature in terms of mismatch compared with the melting temperature for a perfectly matched duplex (See pg. 333, fig5). It would have been prima facie obvious to identify a sequence alteration in a target nucleic acid as compared to a control nucleic acid with a plurality of nucleic acid probes.

Summary

8. No claims are allowable.

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9. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

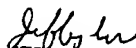
Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

JT

July 11, 2003


JEFFREY SIEW
PRIMARY EXAMINER

7/13/03